REMARKS

Claims 1-20 are pending in this case. No amendments to the claims are made in this response. Please note that an Information Disclosure Statement accompanies this response (with authorization to charge the appropriate fee to a deposit account). The Examiner is respectfully requested to make the documents disclosed therein of record in the instant application, and to return the initialed Form PTO-1449 indicating that the documents have been considered.

The Applicant thanks the Examiner for consideration of the claims as filed, and for the Examiner's comment that no prior art was cited against claims 5, 6, 15-18, and 20.

The claims of the current invention are drawn to treating a disease by administering a therapeutically effective amount of a positron-emitting compound. It is noted in the application that positron emission tomography is a widely-used technique for diagnostic imaging. The amount of positron-emitting substance used for diagnostic imaging is too low to have any appreciable therapeutic effect on a disease, such as a cancerous tumor. Instead, diagnostic imaging using a positron-emitting compound is used, for example, to map the location of a tumor in a subject, and to monitor the effects of a different therapy on the tumor. In contrast, the current invention uses sufficient amounts (therapeutically effective amounts) of a positron-emitting compound, such that the positron-emitting compound itself has a therapeutic effect.

Rejections under 35 U.S.C § 112, 2nd paragraph

Claims 1-20 were rejected under 35 U.S.C § 112, 2nd paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner requested clarification with respect to the terms "disease" and "other chemotherapy or radiation therapy."

The specification indicates that the methods of the invention are particularly useful in treatment of cancer and related diseases (see, inter alia, page 2, lines 20-21, and page 5, lines 20-21. Cancer is of course used to refer to a wide variety of malignant growths. As the hallmark of

cancer is uncontrolled and/or undesirable cell proliferation, one of skill in the art would understand "related diseases" to be diseases marked by uncontrolled and/or undesirable cell proliferation.

"Other chemotherapy or radiation therapy" refers to use of additional modalities of chemotherapy and radiation therapy used for treatment of diseases such as cancer. The method of the invention comprises administration of a therapeutically effective amount of a positron-emitting compound comprising one or more atoms of fluorine-18, carbon-11, nitrogen-13, or oxygen-15. It is a new method of therapy for diseases such as cancer. However, it can be used in conjunction with known therapies, such as administration of known chemotherapeutic compounds or treatment with an external beam of radiation. One of skill in the art would be familiar with a wide variety of chemotherapeutic agents, such as cis-platin, taxol, or doxorubicin, to name a small fraction of well-known drugs, and would also be familiar with radiation therapy, such as external radiation therapy with, e.g., X-rays or gamma rays, and internal radiation therapy with, e.g., implanted radioactive material.

In light of the argument above, it is submitted that the use of the terms "disease" and "other chemotherapy or radiation therapy" in the claims particularly points out and distinctly claims the invention, and accordingly, withdrawal of the rejections under 35 U.S.C. § 112, 2nd paragraph, is respectfully requested.

Rejections under 35 U.S.C. 102(b)

Claims 1, 9-12, 13, 14 and 19 were rejected under 35 U.S.C. 102(b) as being anticipated by McPherson et al. (U.S. Patent No. 4,874,600).

However, McPherson simply discusses imaging techniques in a subject using [1-^{11}C]putrescine, and does not teach or suggest using the [1-^{11}C]putrescine itself as a therapeutic treatment. The treatment discussed in McPherson appears to be standard radiotherapy or chemotherapy (column 1, lines 65-67). In Example 2 at column 4, lines 45-50, McPherson discloses that 0.05-0.20 μCi of [1-^{11}C]putrescine were used per mouse, and that the mice

weighed between 20 g and 32 g. Taking the highest dosage used (0.20 μCi) in the mouse of lowest mass (20 g) (which gives the maximum dosage used), McPherson used a dosage of 0.01 μCi/g, or (multiplying both numerator and denominator by 1000) 0.01 mCi/kg. In a 50-kg animal, this would correspond to 0.50 mCi, that is, one-half of one milliCurie. This is far too low to have any appreciable therapeutic effect, and thus does not fall within the "therapeutically effective amount" limitation of the instant claims. Since the stated aim of McPherson is to image tumors, and the dosage of radiation used in the patent is too low to have any appreciable therapeutic effect on a tumor, it is clear that McPherson does not disclose, either directly or inherently, a method for treating a disease by administering a therapeutically effective amount of [1-^{11}C]putrescine. As claim 1 (and claims 9-12, 13, 14 and 19, dependent on claim 1) recite administration of a therapeutically effective amount of a positron-emitting compound, withdrawal of this rejection is respectfully requested.

Claims 1-4 were rejected under 35 U.S.C. 102(b) as being anticipated by Smith et al. (The Breast, 1999, Vol. 8, pages 303-310).

Again, as in McPherson, the Smith reference is concerned with imaging, and does not disclose the use of positron-emitting compounds as therapeutic agents themselves; Smith simply refers to them as imaging agents used to gauge the effectiveness of other treatments. As 1 milliCurie equals 37 MegaBecquerels, the total dosage referred to in Smith et al. is 20 mCi. This is below the therapeutically effective amount as described in the instant specification; administration of a therapeutically effective amount is recited in instant claim 1, from which claims 2-4 depend. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1-4, 7-14, and 19 were rejected under 35 U.S.C. 102(b) as being anticipated by Paulus et al. (Acta Gastroenterel. Belg., 1997, Vol. 60, pages 278-280).

Paulus discusses the use of fluorodeoxyglucose as an imaging technique, and not as a compound useful for therapeutic treatment in and of itself. The range of 100-400 MBq (about

3-11 mCi), with a typical dose of 300 MBq (about 8.11 mCi) is again too low to have therapeutic effect. In contrast, instant claims 1-4, 7-14, and 19 require administration of a therapeutically effective amount of the positron-emitting compound. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1-4 and 13 were rejected under 35 U.S.C. 102(b) as being anticipated by Schelbert et al. (Cardiology Clinics 1994, Vol. 12, No. 2, pages 303-315).

As in the previous references, Schelbert teaches diagnosing and imaging a disease using certain positron-emitting compounds. Schelbert does not teach administration of a positron-emitting compound in an amount sufficient to have a therapeutic effect, as required by claims 1-4 and 13 of the instant invention. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. 103(a)

Claims 1, 14, and 19 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lemelson (U.S. Patent No. 4,665,897).

While Lemelson's patent is entitled "Composition and Method for Detecting and Treating Cancer," it is clear that the use of positron-emitting radionuclides in Lemelson is limited to imaging techniques. This is specifically indicated immediately prior to one of the sections of Lemelson cited by the Examiner (the Examiner cited column 8, lines 36-57). At column 8, lines 28-36, Lemelson states that "...suitable detection of the site or sites at which the antibodies are located...must be effected to permit the beam or beams of externally generated neutrons to be properly directed through the body of the patient. Such monitoring may be effected by the detection of radiation emitted from the antibodies at the tumor site(s)." Thus, the context of the use of positron-emitting compounds in the Lemelson patent is for <u>imaging</u> of the patient undergoing treatment, in order to direct an external beam of radiation; the positron-emitting substance is <u>not</u> present for the purpose of <u>treating</u> the patient.

In the abstract, also cited by the Examiner, Lemelson indicates that the drug units include a normally inactive nuclide capable of being rendered radioactive for treating a disease, and a second nuclide which may be either inactive or radioactive. The drug units emit radiation after being activated within the body by radiation such as neutrons in order to determine the location and extent of the disease—in other words, to image the disease. Once the disease has been imaged, "nuclide material carried to the detected site may be activated by properly controlling the location of a source of activating radiation, its direction and activation to effect treatment of the disease." Thus the treatment of the disease is accomplished by activating a previously non-radioactive nucleus, not by administering a therapeutically effective amount of a positron-emitting compound (which is already radioactive and does not need to be activated by an external beam).

Column 13, lines 5-18 describes antibodies which may contain "...either the explosive radionuclide and a radioactive nuclide or a nuclide capable of generating detectable radiation per se as described." (Column 13, lines 9-12.) It does not disclose administering positron-emitting compounds; again, carbon-11 and nitrogen-13 are mentioned in the context of imaging (detection), not therapeutic use, in column 8, and thus one would not use those isotopes in therapeutic amounts.

Finally, the remaining sections of Lemelson cited by the Examiner (column 10, line 61 and columns 11-12, bridging paragraph) simply mention treatment in general, without any indication or suggestion to use positron-emitting compounds in a therapeutically effective amount.

As instant claims 1, 14, and 19 require administration of a therapeutically effective amount of a positron-emitting compound, and as Lemelson does not explicitly or implicitly teach or suggest this method, withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant submits that all outstanding issues (rejections under 35 U.S.C. § 112, 2nd paragraph, rejections under 35 U.S.C. 102(b), and rejection under 35 U.S.C. 103(a)) have been addressed in this response. Reconsideration and allowance of the claims in light of the comments herein is earnestly solicited. Should the Examiner have any questions, he is invited to contact the undersigned agent for the Applicant at telephone number 1-213-892-5615.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing 50682-20001.00. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: January 6, 2003

Respectfully submitted,

By: _____

Robert K. Cerpa
Registration No. 39,933

Morrison & Foerster LLP
555 West Fifth Street
Suite 3500
Los Angeles, California 90013-1024
Telephone: (213) 892-5615
Facsimile: (213) 892-5454